Refine Search

Search Results -

Term	Documents
(8 NOT 5).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	84
(L8 NOT L5).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	84

Database: US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L9

Refine Search

Recall Text Clear Interrupt

Search History

DATE: Tuesday, April 04, 2006 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L9	L8 not L5	84	L9
L8	L7 and (pulmonary or lung or intranasal)	95	L8
L7	L6 and L4	142	L7
L6	(Factor adj VIII) and (Hemophilia adj B)	458	L6
L5	L4 same (pulmonary or lung or intranasal)	59	L5
L4	(Factor adj VIII) same (vector)	997	L4
L3	L2 and (Factor adj VIII)	2	L3
L2	Cheng-Seng.in.	4	L2
L1	Li-Chester.in.	2	L1

END OF SEARCH HISTORY

PALM INTRANET

Day : Tuesday
Date: 4/4/2006
Time: 15:02:23

Inventor Name Search

Enter the first few letters of the Inventor's Last Name.
Additionally, enter the first few letters of the Inventor's First name.

Last Name	First Name	
Cheng	Seng	Search

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PALM INTRANET

Day : Tuesday
Date: 4/4/2006
Time: 15:02:23

Inventor Name Search

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Last Name	First Name	
Ziegler	Robin	Search

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PALM INTRANET

Day : Tuesday
Date: 4/4/2006
Time: 15:02:23

Inventor Name Search

Enter the first few letters of the Inventor's Last Name.
Additionally, enter the first few letters of the Inventor's First name.

Last Name	First Name	
Li	Chester	Search

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                    Welcome to DialogClassic Web(tm)
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NEW FILES RELEASED
***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)
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(File 302).
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File   1:ERIC 1966-2006/Feb
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      Set  Items  Description
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Cost is in DialUnits
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B 155, 5, 73
       04apr06 15:28:03 User259876 Session D859.1
            $0.82    0.233 DialUnits File1
     $0.82  Estimated cost File1
     $0.05  INTERNET
     $0.87  Estimated cost this search
     $0.87  Estimated total session cost   0.233 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1951-2006/Apr 04
         (c) format only 2006 Dialog
 *File 155: Medline has been reloaded. Some accession numbers
have changed.
  File   5:Biosis Previews(R) 1969-2006/Mar W4
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          (c) 2006 BIOSIS
  File  73:EMBASE 1974-2006/Apr 04
          (c) 2006 Elsevier Science B.V.

      Set   Items   Description
      ---   -----   -----------
?

S (HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
              84   HEMOPHILA
         2238482   B
         5811769   THERAPY
         5097651   TREATMENT
      S1       2   (HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
?

RD
      S2       2   RD  (unique items)
?

T S2/3,K/ALL

  2/3,K/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0007878455   BIOSIS NO.: 199192124226
 EXPRESSION OF HUMAN FACTOR IX IN RAT CAPILLARY ENDOTHELIAL CELLS TOWARD
 SOMATIC GENE THERAPY FOR HEMOPHILIA B
AUTHOR: YAO S-N (Reprint); WILSON J M; NABEL E G; KURACHI S; HACHIYA H L;
  KURACHI K
AUTHOR ADDRESS: DEP HUMAN GENETICS, UNIV MICHIGAN MED SCH, ANN ARBOR, MICH
  48109-0618, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United
States of America  88 (18): p8101-8105 1991
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

...ABSTRACT: and direct contact with the circulating blood, suggest that
  CECs can serve as an efficient drug delivery vehicle producing factor IX
  in a somatic gene therapy for hemophilia B.


  2/3,K/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0007310757   BIOSIS NO.: 199090095236
 EXPRESSION OF HUMAN FACTOR IX IN RABBIT HEPATOCYTES BY RETROVIRUS-MEDIATED
 GENE TRANSFER POTENTIAL FOR GENE THERAPY OF HEMOPHILIA B
AUTHOR: ARMENTANO D (Reprint); THOMPSON A R; DARLINGTON G; WOO S L C
AUTHOR ADDRESS: HOWARD HUGHES MEDICAL INST, DEP CELL BIOLOGY, BAYLOR COLL
  MED, HOUSTON, TEXAS 77030, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United
States of America  87 (16): p6141-6145 1990
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
```

LANGUAGE: ENGLISH

...ABSTRACT: assays. These results establish the feasibility of using infected hepatocytes for the expression of this protein and are a step toward the goal of correcting **hemophila B** by hepatic gene transfer.
?

```
Set     Items   Description
S1          2   (HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
S2          2   RD  (unique items)
?

(FACTOR (W) VIII) (S) (VECTOR)
>>>When using accession numbers with KEEP in OneSearch, you
>>>must use the FROM option to specify a file number.
?

S (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
        2511338  FACTOR
          87314  VIII
         305693  VECTOR
         205496  PLASMID
      S3    457  (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
?

S S3  (S) (PULMONARY OR LUNG OR INTRANASAL)
            457  S3
        1118201  PULMONARY
        1137972  LUNG
          38141  INTRANASAL
      S4     21  S3  (S) (PULMONARY OR LUNG OR INTRANASAL)
?

S S4 AND (HEMOPHILIA (W) B)
             21  S4
          36686  HEMOPHILIA
        2238482  B
           6542  HEMOPHILIA(W)B
      S5      0  S4 AND (HEMOPHILIA (W) B)
?

RD S4
      S6     11  RD S4  (unique items)
?

T S6/3,K/ALL

  6/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

19760175   PMID: 16361563
 Overexpression of stefin A in human esophageal squamous cell carcinoma
 cells inhibits tumor cell growth, angiogenesis, invasion, and metastasis.
  Li Wendong; Ding Fang; Zhang Liyong; Liu Zhongmin; Wu Yu; Luo Aiping; Wu
Min; Wang Mingrong; Zhan Qimin; Liu Zhihua
  National Laboratory of Molecular Oncology, Cancer Institute, Chinese
Academy of Medical Sciences and Peking Union Medical College, Beijing, P.R.
China.
```

Clinical cancer research - an official journal of the American Association for Cancer Research (United States) Dec 15 2005, 11 (24 Pt 1) p8753-62, ISSN 1078-0432--Print Journal Code: 9502500
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... cathepsin B activity and inhibited the Matrigel invasion. Overexpression of stefin A delayed the in vitro and in vivo growth of cells and significantly inhibited **lung** metastasis compared with 50% of **lung** metastasis in xenograft mice from EC9706 or empty **vector** cells. Transfection with stefin A showed a dramatic reduction of **factor VIII** staining in the tumors of xenograft mice. CONCLUSIONS: Our data strongly indicate that stefin A plays an important role in the growth, angiogenesis, invasion, and...

6/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14901673 PMID: 15157331
[In vivo transfection and expression of human coagulant factor VIII cDNA in mice]
Kang Wen-Ying; Wang Hong-Li; Wang Hong; Wang Xue-Feng; Wang Cong-Zhu; Fu Qi-Hua; Ding Qiu-Lan; Wu Wen-Man; Fang Yi; Wang Zhen-Yi
Shanghai Institute of Hematology, Ruijin Hospital, The Shanghai Second Medical University, Shanghai 200025, China.
Zhongguo shi yan xue ye xue za zhi / Zhongguo bing li sheng li xue hui = Journal of experimental hematology / Chinese Association of Pathophysiology (China) Apr 2004, 12 (2) p188-93, ISSN 1009-2137--Print
Journal Code: 101084424
Publishing Model Print
Document type: Journal Article ; English Abstract
Languages: CHINESE
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The aim is to observe the expression of human factor VIII gene in mice tranduced in vivo and ex vivo. The **vector** pLNC-FVIII BD was generated by cloning a B-domain-deleted (760aa-1639aa) FVIII cDNA (FVIIIBD cDNA) into retroviral **vector** pLNCX. 2 x 10(6) of mouse bone marrow stroma cells transduced by LNC-FVIII BD were infused into 4-week-old BALB/c mice...

...l contained 15 micro g/mouse) and sacrificed at days 1, 2, 7, 14, 21 and 28, respectively after injection. Tissue such as liver, spleen, **lung** and kindney were harvested, with which the transcription were detected by means of RT-PCR. In addition, blood was collected to be measured human FVIII...

... inhibitors was not revealed all the time. Syngene image scanning demonstrated that the transcription of the human FVIII BD cDNA occurred mainly in spleen and **lung** , and secondarily in liver and kidney. No side effects of PAMAM-pLNC-FVIII BD were observed in mice tissue by pathological examination at 4 weeks...

6/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14495641 PMID: 12714372

Lung overexpression of angiostatin aggravates pulmonary hypertension in chronically hypoxic mice.

Pascaud Marie-Aude; Griscelli Frank; Raoul William; Marcos Elisabeth; Opolon Paule; Raffestin Bernadette; Perricaudet Michael; Adnot Serge; Eddahibi Saadia

INSERM U492, Faculte de Medecine, 8 Rue du General Sarrail, 94010 Creteil, France. eddahibi@im3.inserm.fr

American journal of respiratory cell and molecular biology (United States) Oct 2003, 29 (4) p449-57, ISSN 1044-1549--Print Journal Code: 8917225

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... 2.4 versus 30.2 +/- 1.4, respectively), aggravation of right ventricular hypertrophy (P < 0.05), and muscularization of distal vessels (P < 0.01). Lung **factor VIII** , CD31 immunostaining, as well as eNOS expression were significantly increased after exposure to hypoxia in Ad.CO1-pretreated controls, but decreased in both normoxic and hypoxic animals after treatment with Ad.K3. The results show that inhibition of hypoxia-induced stimulation of **lung** angiogenic processes aggravates development of hypoxic PH. This suggests that endogenous **lung** angiogenesis counteracts development of hypoxic PH.

6/3,K/4 (Item 4 from file: 155)

13749347 PMID: 12015067

[Preliminary experimental research on gene therapy for hemophilia A]

Yin Jun; Wang Hongli; Hu Yiqun; Wang Xuefeng; Qu Bin; Chu Haiyan; Duan Baohua; Kang Wenying; Qi Zhengwu; Wang Zhenyi

Shanghai Institute of Hematology, Ruijin Hospital, Shanghai Second Medical University, Shanghai 200025, China.

Zhonghua xue ye xue za zhi = Zhonghua xueyexue zazhi (China) Mar 2002, 23 (3) p138-42, ISSN 0253-2727--Print Journal Code: 8212398

Publishing Model Print

Document type: Journal Article ; English Abstract

Languages: CHINESE

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... expression of human factor VIII (hF VIII) in vivo. METHODS: Human clotting factor VIII cDNA with B-domain deleted (Delta760aa approximately 1639aa) was inserted into **vector** pRC/RSV to form pRC/RSV-hF VIII BD, which conjugated with in vivo liposome transfection reagent (DOTAP-Cholesterol) to accomplish a kind of therapeutic...

... i.m. and sacrificed 48 hours, 10 days, 20 days, 30 days, 40 days and 50 days later, respectively. Tissues such as heart, liver, spleen, **lung** , kidney and muscle were harvested, the distribution and transcription as well as expression of hF VIII BD cDNA were detected by means of PCR, RT...

6/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12472710 PMID: 10418799
The gene expression of coagulation factor VIII in mammalian cell lines.
Chen C; Fang X D; Zhu J; Wu X F; Zhang Z C; Gu J X; Wang Z Y; Chi C W
Shanghai Institute of Biochemistry, Academia Sinica, China.
Thrombosis research (UNITED STATES) Jul 15 1999, 95 (2) p105-15,
ISSN 0049-3848--Print Journal Code: 0326377
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... is specific for cells from different tissues. The highest expression level was found in the hepatocellular carcinoma line SMMC-7721, followed by kidney, ovary, and **lung** cell lines. To compare the efficiency of gene expression of recombinant **factor VIII** , the **factor VIII** -deltaB gene was further reconstructed in different forms in the expression **plasmid** pCMV-dhfr for transient gene expression in Chinese hamster ovary cells. The redundant 5'- and 3'-untranslated sequences of **factor VIII** -deltaB were deleted. The cDNA encoding the heavy and light chains of **factor VIII** were constructed, respectively. Among them the high yield of the recombinant **factor VIII** was found in the coexpression of the heavy and light chain cDNA fragments of **factor VIII** . The deletion of the redundant 5'-untranslated sequence of **factor VIII** -deltaB was also beneficial for gene expression. As expected, the gene coexpression of **factor VIII** -deltaB and von Willibrand Factor cloned by the long-polymerase chain reaction method was also helpful for enhancing the expression level of recombinant **factor VIII** . A monoclonal antibody raised against **factor VIII** was prepared and used for the specific assay of recombinant **factor VIII** by the competitive ELISA method, the assay results were consistent with those determined by the one-stage bioassay.

6/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11533784 PMID: 9367354
Development of immortalized human cerebromicrovascular endothelial cell line as an in vitro model of the human blood-brain barrier.
Muruganandam A; Herx L M; Monette R; Durkin J P; Stanimirovic D B
Cellular Neurobiology Group, Institute of Biological Sciences, National Research Council of Canada, Ottawa, Ontario.
FASEB journal - official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) Nov 1997, 11 (13) p1187-97, ISSN 0892-6638--Print Journal Code: 8804484
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... specific enzymes alkaline phosphatase and gamma-glutamyl transpeptidase. The diffusion of radiolabeled sucrose across SV-HCEC monolayers was fivefold lower than that observed with human **lung** microvascular endothelial cells. Furthermore, media conditioned by fetal

human astrocytes increased the transendothelial electrical resistance of SV-HCEC monolayers by 2.5-fold. Therefore, this...

6/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11380850 PMID: 9264782
[Genetic therapy for hemophiliacs--therapeutic potential and technological limits]
Therapie genique des hemophilies--potentialites therapeutiques et limitations technologiques.
Michou A I; Christ M; Pavirani A; Mehtali M
Transgene S.A., Strasbourg, France.
Transfusion clinique et biologique - journal de la Societe francaise de transfusion sanguine (FRANCE) 1997, 4 (3) p251-61, ISSN 1246-7820--Print Journal Code: 9423846
Publishing Model Print
Document type: Journal Article; Review ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... transfer protocol for haemophilia B, we constructed and tested in vitro and in vivo various recombinant adenovirus vectors expressing human FIX. Intravenous administration of this **vector** into various strains of immunocompetent and immunodeficient mice led to an efficient hFIX gene transfer in liver and **lung** . As a consequence, the hFIX protein was correctly produced and secreted at high levels in the blood of the treated animals. However, expression was transient...

6/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11229023 PMID: 9816156
Interleukin 10 suppresses tumor growth and metastasis of human melanoma cells: potential inhibition of angiogenesis.
Huang S; Xie K; Bucana C D; Ullrich S E; Bar-Eli M
Departments of Cell Biology and Immunology, The University of Texas Anderson Cancer Center, Houston, Texas 77030, USA.
Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Dec 1996, 2 (12) p1969-79, ISSN 1078-0432--Print Journal Code: 9502500
Contract/Grant No.: AR 40824; AR; NIAMS; CA 41525; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... c. injection into nude mice. The suppression of tumor growth and metastasis was directly correlated with a decrease in neovascularity determined by immunostaining with anti- **factor VIII** . Because tumor-associated macrophages are the major source of angiogenic molecules in melanoma, we used reverse transcription-PCR to demonstrate that IL-10 down-regulates...

6/3,K/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09624416 PMID: 7683277
Immortalization of epithelial-like cells from human liver tissue with SV40 T-antigen gene.
Miyazaki M; Mihara K; Bai L; Kano Y; Tsuboi S; Endo A; Seshimo K; Yoshioka T; Namba M
Department of Cell Biology, Okayama University Medical School, Japan.
Experimental cell research (UNITED STATES) May 1993, 206 (1) p27-35, ISSN 0014-4827--Print Journal Code: 0373226
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... were sensitive to cytotoxicity of aflatoxin B1, 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole, and benzo[a]pyrene, whereas human embryo **lung** fibroblasts were insensitive to the cytotoxicity of these carcinogens. These findings suggest that OUMS-21 and -22 cells may arise from undifferentiated liver stem cells...

6/3,K/10 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010232509 BIOSIS NO.: 199698700342
Construction of metallothionein-I promoter inserted human blood coagulation factor VIII expression vector and the induction of factor VIII protein synthesis in mouse
AUTHOR: Oh Sang-Hwan (Reprint); Kim Seok-Hyun; Min Yoo-Hong; Kim Young-Soo; Kim Yoon-Soo
AUTHOR ADDRESS: Dep. Biochem. Mol. Biol., Inst. Genetic Sci., Yonsei Univ. Coll. Med., Seoul 120-752, South Korea**South Korea
JOURNAL: Korean Journal of Biochemistry 27 (4): p199-208 1995 1995
ISSN: 0378-8512
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: a recombinant human blood coagulation factor VIII (FVIII) has been attempted by the construction of a mouse metallothionein-I (MT-I) promoter driven eukaryotic expression **vector** system, in order to test the metal-regulated synthesis of FVIII in vivo. For the construction of the MT-I promoter directed FVIII expression **vector** (pMTVIII-B), MT-I promoter sequence was substituted with CMV early promoter in pCMV **vector** and B-domain deleted FVIII cDNA sequence was inserted to the downstream of MT-I promoter. pMTVIII-B was cotransfected with pRSVneo into Chinese hamster...

...pMTVIII-B. Administration of Zn (1 mg/30 g body weight) to mice transfused with pMTVIII-B increased FVIII-B expression in liver, spleen and **lung** of mice, and the presence of FVIII in the liver of mice was confirmed by immunohistochemical staining. These results suggest that MT-I promoter driven FVIII-B expression **vector** system may be useful for the synthesis and secretion of biologically active recombinant FVIII in

vivo.

6/3,K/11 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

06909878 EMBASE No: 1997194320
Gene therapy for hemophiliacs - Therapeutic possibilities and technological limits
THERAPIE GENIQUE DES HEMOPHILIES - POTENTIALITES THERAPEUTIQUES ET LIMITATIONS TECHNOLOGIQUES
Michou A.I.; Christ M.; Pavirani A.; Mehtali M.
M. Mehtali, Transgene S.A., 11 Rue de Molsheim, 67000 Strasbourg France
Transfusion Clinique et Biologique (TRANSFUS. CLIN. BIOL.) (France)
1997, 4/3 (251-261)
CODEN: TCBIF ISSN: 1246-7820
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: FRENCH SUMMARY LANGUAGE: FRENCH; ENGLISH
NUMBER OF REFERENCES: 25

Defects in the genes encoding the human coagulation **factor VIII** (hFVIII) and IX (hFIX) result in life-threatening haemorrhages and severe arthropathies. While haemophiliacs are currently treated by blood-derived factors or recombinant hFVIII and...

...transfer protocol for haemophilia B, we constructed and tested in vitro and in vivo various recombinant adenovirus vectors expressing human FIX. Intravenous administration of this **vector** into various strains of immunocompetent and immunodeficient mice led to an efficient hFIX gene transfer in liver and **lung** . As a consequence, the hFIX protein was correctly produced and secreted at high levels in the blood of the treated animals. However, expression was transient...
?

Set	Items	Description
S1	2	(HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
S2	2	RD (unique items)
S3	457	(FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
S4	21	S3 (S) (PULMONARY OR LUNG OR INTRANASAL)
S5	0	S4 AND (HEMOPHILIA (W) B)
S6	11	RD S4 (unique items)

?

```
S S3 AND (HEMOPHILIA (W) B)
             457  S3
           36686  HEMOPHILIA
         2238482  B
            6542  HEMOPHILIA(W)B
      S7      30  S3 AND (HEMOPHILIA (W) B)
?

S S7 AND (PULMONARY OR LUNG OR INTRANASAL)
              30  S7
         1118201  PULMONARY
         1137972  LUNG
           38141  INTRANASAL
      S8       0  S7 AND (PULMONARY OR LUNG OR INTRANASAL)
?
```

```
Set      Items   Description
S1           2   (HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
S2           2   RD  (unique items)
S3         457   (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
S4          21   S3  (S) (PULMONARY OR LUNG OR INTRANASAL)
S5           0   S4 AND (HEMOPHILIA (W) B)
S6          11   RD S4  (unique items)
S7          30   S3 AND (HEMOPHILIA (W) B)
S8           0   S7 AND (PULMONARY OR LUNG OR INTRANASAL)
?

RD S7
      S9       19  RD S7  (unique items)
?

S S9 NOT S6
               19  S9
               11  S6
     S10       19  S9 NOT S6
?

T S10/3,K/ALL
```

10/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
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15574896 PMID: 16096011

A novel gene expression system: non-viral gene transfer for hemophilia as model systems.

Miao Carol H

Department of Pediatrics, University of Washington and Children's Hospital and Regional Medical Center, Seattle, Washington 98195, USA.

Advances in genetics (United States) 2005, 54 p143-77, ISSN 0065-2660--Print Journal Code: 0370421

Contract/Grant No.: HL69409-02; HL; NHLBI

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... integrating vectors. Using in vivo screening of vectors incorporating many different combinations of gene regulatory sequences, liver-specific, high-expressing vectors to accommodate factor IX, **factor VIII** , and other genes for effective gene transfer have been established. Persistent and high levels of factor IX and **factor VIII** gene expression for treating **hemophilia B** and A, respectively, were achieved in mouse livers using hydrodynamics-based gene transfer of naked **plasmid** DNA incorporating these novel gene expression systems. Some other systems to prolong or stabilize the gene expression following gene transfer are also discussed.

10/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

15514588 PMID: 15975012
AAV-mediated gene transfer for treatment of hemophilia.
Wang Lixin; Herzog Roland W
Dept. Pediatrics, University of Pennsylvania Medical Center, The Children's Hospital of Philadelphia, Philadelphia, PA 19104, USA.
Current gene therapy (Netherlands) Jun 2005, 5 (3) p349-60, ISSN 1566-5232--Print Journal Code: 101125446
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

...of two Phase I/II clinical trials to evaluate the safety of AAV-factor IX gene transfer to muscle and liver of patients with severe **hemophilia B** . Herein, we have reviewed results from studies in animals with hemophilia, early experience with the **vector** system in the clinic, recent innovative approaches in **vector** design and delivery, and strategies to circumvent immunological limitations. Taken together, these studies provide much encouragement for the possibility of future clinical success, but also ...

10/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

15143362 PMID: 15508114
Gene therapy of the hemophilias.
Lozier Jay
Food and Drug Administration Center for Biologics Evaluation and Research, Rockville, MD 20852-1448, USA. lozier@cber.fda.gov
Seminars in hematology (United States) Oct 2004, 41 (4) p287-96, ISSN 0037-1963--Print Journal Code: 0404514
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... dogs) more closely replicate the requirements for correction of human hemophilia than do mice. Small animals are more convenient to maintain and require significantly less **vector** for testing than do large animals. Nonhemophilic animals (mice or nonhuman primates), whose endogenous **factor VIII** and factor IX complicate analysis of the human proteins, have utility for safety testing of vectors; some assays can discriminate between human coagulation factors and the endogenous coagulation factors. Most animal models suffer the limitations imposed by the immune response to human **factor VIII** or IX protein. Clinical trials have failed to achieve significant **factor VIII** expression in hemophilia A patients, while one clinical trial in **hemophilia B** patients showed only transient therapeutic increments of factor IX expression. Gene therapy remains an investigational method with many obstacles to overcome before it can be...
Descriptors: *Gene Therapy--methods--MT; **Hemophilia B** --therapy--TH

10/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14817480 PMID: 15057309
Novel therapeutic approach for hemophilia using gene delivery of an engineered secreted activated Factor VII.
Margaritis Paris; Arruda Valder R; Aljamali Majed; Camire Rodney M; Schlachterman Alexander; High Katherine A
Division of Hematology, The Children's Hospital of Philadelphia, Abramson Research Center, Philadelphia, Pennsylvania 19104, USA.
Journal of clinical investigation (United States) Apr 2004, 113 (7) p1025-31, ISSN 0021-9738--Print Journal Code: 7802877
Contract/Grant No.: K01-060580; PHS; U01-HL66948; HL; NHLBI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

...However, its high cost and short half-life have limited its use. Here, we report a novel treatment strategy with a recombinant adeno-associated virus **vector** delivering a modified FVII transgene that can be intracellularly processed and secreted as activated FVII (FVIIa). We show long-term expression, as well as phenotypic correction of **hemophilia B** mice following gene transfer of the murine FVIIa homolog, with no evidence of thrombotic complications at these doses. These data hold promise for a potential...
; Animals; Factor VIIa--metabolism--ME; **Hemophilia B** --therapy--TH; Humans; Mice; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Time Factors

10/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14327287 PMID: 12776156
Gene therapy progress and prospects: gene therapy for the hemophilias.
Walsh Christopher E
Mt Sinai School of Medicine, One Gustave Levy Place, Rm 24-42C Annenberg Building, New York City, NY 10029, USA.
Gene therapy (England) Jun 2003, 10 (12) p999-1003, ISSN 0969-7128 --Print Journal Code: 9421525
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... for hemophilia gene transfer require the long-term therapeutic production of the coagulant protein without stimulating an immune response to the transgene product or the **vector** . Based on a scientific understanding of the molecular and cellular defects, leading to the bleeding phenotype, impressive strides have been made in the last 2...
Descriptors: *Gene Therapy--methods--MT; *Hemophilia A--therapy--TH; *
Hemophilia B --therapy--TH

10/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14085436 PMID: 12544490

AAV-mediated gene transfer for hemophilia.
High Katherine
University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, 19104, USA.
Genetics in medicine - official journal of the American College of Medical Genetics (United States) Nov-Dec 2002, 4 (6 Suppl) p56S-61S, ISSN 1098-3600--Print Journal Code: 9815831
Contract/Grant No.: P01 HL64190; HL; NHLBI; R01 HL61921; HL; NHLBI; U01 HL66948; HL; NHLBI
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... method of treating hemophilia, an inherited bleeding disorder that results from the absence of functional factor VIII or factor IX. Using an adeno-associated viral **vector** derived from AAV serotype 2, we have shown in mice and in hemophilic dogs that we can achieve long-term expression (>3 years) of clotting...
... skeletal muscle results in factor levels of only 1% to 2%. Based on these results, a trial of AAV-mediated liver-directed gene transfer for **hemophilia B** has been proposed and is reviewed here.

10/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14039997 PMID: 12463593
Adeno-associated virus-mediated gene transfer for hemophilia B□.□
High Katherine A
Division of Hematology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania 19104, USA. high@email.chop.edu
International journal of hematology (Ireland) Nov 2002, 76 (4) p310-8, ISSN 0925-5710--Print Journal Code: 9111627
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Adeno-associated virus-mediated gene transfer for hemophilia B□.□
Hemophilia is the bleeding diathesis caused by mutations in the gene encoding factor VIII (hemophilia A) or factor IX (**hemophilia B**). Currently, the disease is treated by intravenous infusion of the missing purified clotting factor. The goal of gene transfer for treating hemophilia is to achieve...

... of AAV. In a staged approach, AAV-factor IX (AAV-F.IX) was first administered at doses of up to 1.8 x 10(12) **vector** genomes/kg (vg/kg) into the skeletal muscles of men with **hemophilia B** . This trial established the safety of parenteral administration and also showed that general characteristics of AAV transduction were similar in mice, dogs, and humans. In an ongoing trial, AAV-F.IX is being administered into the hepatic circulation of men with severe **hemophilia B** . The goal of these studies is to identify a safe dose that reliably yields circulating levels of factor IX >2% of normal levels in all subjects. This goal has already been achieved in the **hemophilia B** dog model; the ongoing study will determine whether a similar result can be achieved in humans with

hemophilia B .
Descriptors: *Gene Transfer Techniques; **Hemophilia B** --therapy--TH

10/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13583637 PMID: 12174674
Gene therapy for hereditary hematological disorders.
Herzog R W; Hagstrom J N
Department of Pediatrics, Children's Hospital of Philadelphia, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania, USA. rwherzog@mail.med.upenn.edu
American journal of pharmacogenomics - genomics-related research in drug development and clinical practice (New Zealand) 2001, 1 (2) p137-44, ISSN 1175-2203--Print Journal Code: 100967746
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... utilizing either an ex vivo, non-viral gene transfer technique or an intravenous infusion of a retroviral vector to treat adults with severe hemophilia A (**factor VIII** deficiency). The third study involves intramuscular administration of an adeno-associated viral (AAV) **vector** for expression of factor IX in adult patients with **hemophilia B** . Results from this study and from preclinical studies preceding the trial demonstrate that it is possible to safely administer high doses of a viral **vector** in vivo.

10/3,K/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13581720 PMID: 12109144
Viral vector-mediated gene therapy for hemophilia.
VandenDriessche T; Collen D; Chuah M K
Center for Transgene, Technology and Gene Therapy, Flanders Interuniversity Institute for Biotechnology, University of Leuven, 49 Herestraat B-3000 Leuven, Belgium. thierry.vandendriessche@med.kuleuven.ac.be
Current gene therapy (Netherlands) Sep 2001, 1 (3) p301-15, ISSN 1566-5232--Print Journal Code: 101125446
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

...Significant progress has been made recently in the development of gene therapy for hemophilia. This has been primarily due to the technical improvements of existing **vector** systems and the development of new gene delivery methods. Therapeutic and sometimes physiologic levels of FVIII and FIX could be achieved in FVIII- and FIX...
Descriptors: *Gene Therapy; *Genetic Vectors; *Hemophilia A--therapy--TH; * **Hemophilia B** --therapy--TH; Adenoviridae--genetics--GE; Animals; Clinical Trials, Phase I; Dependovirus--genetics--GE; Dogs; Factor IX

--genetics--GE; Factor VIII--genetics--GE; Hemophilia A--genetics--GE; **Hemophilia B** --genetics--GE; Humans; Lentivirus--genetics--GE; Mice; Moloney murine leukemia virus--genetics--GE

10/3,K/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13148656 PMID: 11269333
Gene therapy for hemophilia.
Chuah M K; Collen D; VandenDriessche T
Center for Transgene Technology and Gene Therapy, Flanders Interuniversity Institute for Biotechnology, University of Leuven, Belgium.
journal of gene medicine (England) Jan-Feb 2001, 3 (1) p3-20, ISSN 1099-498X--Print Journal Code: 9815764
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... recently been made in the development of gene therapy for the treatment of hemophilia A and B. These advances parallel the technical improvements of existing **vector** systems including MoMLV-based retroviral, adenoviral and AAV vectors, and the development of new delivery methods such as lentiviral vectors, helper-dependent adenoviral vectors and...

... are currently ongoing in patients suffering from severe hemophilia A or B. No significant adverse side-effects were reported, and semen samples were negative for **vector** sequences by sensitive PCR assays. Most importantly, some subjects report fewer bleeding episodes and occasionally have very low levels of clotting factor activity detected. The...
Descriptors: *Gene Therapy; *Hemophilia A--therapy--TH; * **Hemophilia B** --therapy--TH

10/3,K/11 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015576654 BIOSIS NO.: 200510271154
A novel deletion in the FVIIIB-domain that reduces transgene size while preserving FVIII activity
AUTHOR: Liu Yi-Lin (Reprint); Zhu Hua; Schlachterman Alexander; Chang Heesoon; Camire Rodney M; High Katherine A
AUTHOR ADDRESS: Childrens Hosp, Philadelphia, PA 19104 USA**USA
JOURNAL: Blood 104 (11, Part 1): p869A NOV 16 2004 2004
CONFERENCE/MEETING: 46th Annual Meeting of the American-Society-of-Hematology San Diego, CA, USA December 04 -07, 2004; 20041204
SPONSOR: Amer Soc Hematol
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: good target disease for gene therapy. Adeno-associated virus (AAV) vectors have proven successful for the delivery of the factor IX gene in humans with **hemophilia B** . For the treatment of hemophilia A,

a problem in the packaging of the rFVIII cDNA or various B-domainless derivatives (i.e. rFVIII-SQ) in...
...a 4-8-fold increase in specific activity compared to FVIII-SQ. We further tested whether FVIII-RKR could function in an in vivo setting. **Plasmid** DNA (50 mu g) containing FVIII-RKR or FVIII-SQ with liver-specific mouse transthyretin (mTTR) promoter were introduced into hemophilia A (HA) mice hydrodynamically...

...expression cassette of mTTR promoter and FVIII-SQ have been administered. Expression of physiological FVIII levels was observed in high dose group (4.0E+12 **vector** genome per animal, n=4). FVIII activity averages 1.88 U/ml by Coamatic assay or 0.81 U/ml by aPTT assay at 12 weeks post injection. In low dose group (1.0E+12 **vector** genome per animal, n=5) therapeutic level of FVIII is achieved, 0.59 U/ml by Coamatic assay or 0.23 U/ml by aPTTassay...

...and shown to have similar packaging efficiency to AAV-FVIII-SQ. Studies are currently underway with AAV-FVIII-RKR to evaluate the ability of this **vector** to drive long-term expression of functional protein. In summary, we developed a novel FVIII molecule that has high specific activity and is suitable for...

10/3,K/12 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013627016 BIOSIS NO.: 200200220527
Long-term expression of activated FVII in vivo following AAV-mediated liver gene transfer: Implications for treatment with continuous infusion of recombinant activated FVII
AUTHOR: Margaritis Paris (Reprint); Arruda Valder R (Reprint); High Katherine A (Reprint)
AUTHOR ADDRESS: Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA, USA**USA
JOURNAL: Blood 98 (11 Part 1): p696a November 16, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: be used in a hemophilic mouse model. To further study the long-term effect of continuous FVIIa expression, we constructed a recombinant AAV-2 viral **vector** carrying this FVIIa transgene under the control of a liver-specific promoter and injected **vector** into the portal circulation in hemostatically normal immunodeficient mice (n=7) at doses ranging from 1.5X1011 **vector** genomes (v.g.)/mouse to 2.4X1012 v.g./mouse. Mouse plasma was collected and assayed for antigen levels by an ELISA specific for human...
DESCRIPTORS:
...DISEASES: **hemophilia B** --
...MESH TERMS: **Hemophilia B** (MeSH)

10/3,K/13 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013627009 BIOSIS NO.: 200200220520

Induction of immunological tolerance to a coagulation factor antigen by hepatic gene transfer

AUTHOR: Mingozzi Federico (Reprint); Arruda Valder R (Reprint); Liu Yi-Lin (Reprint); Wang YuQuin (Reprint); Liu Jian Hua (Reprint); Kaufhold Antje (Reprint); High Katherine A (Reprint); Herzog Roland W (Reprint)
AUTHOR ADDRESS: Pediatrics and Pathology, Childrens Hospital of Philadelphia and University of Pennsylvania Medical Center, Philadelphia, PA, USA**USA

JOURNAL: Blood 98 (11 Part 1): p694a November 16, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: therapy is an attractive alternative to conventional treatment of hemophilia, because efficient and sustained expression of factor VIII (hemophilia A) or factor IX (F.IX, **hemophilia B**) would provide a continuous supply of factor. A potentially serious complication of treatment is the formation of neutralizing antibody (inhibitor) against the coagulation factor. It...

...17 months, experiment ongoing) of canine F.IX (at levels of 5-12% of normal) after adeno-associated virus (AAV)-mediated hepatic gene transfer in **hemophilia B** dogs with a F.IX null mutation. Animals of this strain without exception formed inhibitors in other gene replacement strategies. Here, we demonstrate in murine models that hepatic AAV-F.IX transduction following introduction of **vector** into the portal circulation can induce tolerance to the expressed F.IX antigen. Normal mice of 4 different strains (C57BL/6, BALB/c, C3H, CD-1) received AAV **vector** expressing human F.IX (hF.IX) from the EF1alpha promoter (n=4 per strain, 1-3X1011 **vector** genomes/mouse) by splenic capsule injection. Except for CD-1 mice that formed anti-hF.IX by 4 weeks, mice of all other strains showed...

...hepatocyte-derived expression of the antigen is likely sufficient for tolerance induction. Interestingly, naive mice formed high titer anti-hF.IX after introduction of the **vector** to skeletal muscle indicating that the tolerizing effect of gene transfer is dependent on the target tissue. Anti-hF.IX formation in CD-1 mice...

...observed for the other strains), but mostly Th1-driven after hepatic gene transfer suggesting differences in activation of CD4+ T helper cells in these tissues. **Hemophilia B** mice (BALB/c or C3H background) with no endogenous F.IX expression formed anti-hF.IX after gene transfer, albeit transiently in some animals, but showed sustained expression without anti-F.IX formation when the species-specific murine F.IX transgene was used. This treatment was also successful in **hemophilia B** /CD-1 mice. Since our observations were not limited to a particular strain of mice, AAV-mediated hepatic gene transfer may generally be useful for inducing tolerance to a F.IX antigen. Therefore, these results are encouraging for in vivo administration of AAV vectors to **hemophilia B** patients with severe F.IX mutations, and illustrate the potential of gene transfer as a tool for induction of antigen-specific immune

tolerance.
DESCRIPTORS:
DISEASES: **hemophilia B** --
MESH TERMS: **Hemophilia B** (MeSH)

10/3,K/14 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013139633 BIOSIS NO.: 200100311472
In utero delivery of AD-CMV-HFIX results in correction of hemophilia B **in the neonatal period**
AUTHOR: Lipshutz Gerald S (Reprint); Wang Lili; Gaensler Karin M L (Reprint)
AUTHOR ADDRESS: Medicine and Surgery, University of California, San Francisco, CA, USA**USA
JOURNAL: Blood 96 (11 Part 2): p387b November 16, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000; 20001201
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

In utero delivery of AD-CMV-HFIX results in correction of hemophilia B **in the neonatal period**

ABSTRACT: **Hemophilia B** affects about 1 in 25,000 males. Severely affected neonates are at increased risk for catastrophic perinatal bleeding. Recent advances in the development of factor...

...likely to occur with vector-derived factor IX expression in adult patients. The development of strategies for the induction of immune tolerance to factor IX, **factor VIII** , and other therapeutic proteins will be important for the future success of gene therapy-based treatments for genetic disorders. In this study, we have assessed whether therapeutic levels of factor IX could be produced in a murine model of **hemophilia B** after injection of a viral gene delivery **vector** prenatally. An adenoviral human factor IX (HFIX) **vector** (Ad-HFIX) was generated by initially subcloning full length HFIX (provided by Darrel W. Stafford, University of North Carolina) between a CMV promoter and SV40 polyadenylation signal. This construct was subcloned into a shuttle **plasmid** before co-transfecting 293 cells with a serotype 5, E1- and E3-deleted replication-deficient recombinant adenoviral **plasmid** . **Hemophilia B** carrier female mice (XHX) produced by a targeted disruption of the murine factor IX gene (provided by Inder Verma, Salk Institute) were bred with XHY...
DESCRIPTORS:
...DISEASES: **hemophilia B** --
MESH TERMS: **Hemophilia B** (MeSH)

10/3,K/15 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12607027 EMBASE No: 2004199158

Preclinical animal models for hemophilia gene therapy: Predictive value and limitations

Rawle F.E.M.; Lillicrap D.
Dr. D. Lillicrap, Dept. of Pathol. and Molec. Medicine, Richardson Laboratory, Queen's University, Kingston, Ont. K7L 3N6 Canada
AUTHOR EMAIL: lillicrap@cliff.path.queensu.ca
Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (205-213)
CODEN: STHMB ISSN: 0094-6176
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 57

...design of gene therapy protocols, and over the last 5 years it has been shown that long-term phenotypic correction, with sustained therapeutic levels of **factor VIII** (FVIII) and factor IX (FIX), can be attained in FVIII- and FIX-deficient mice and dogs using various viral **vector** -mediated gene therapy approaches. These animal models also have elucidated potential complications of gene therapy protocols, including acute **vector** -associated toxicities and the induction of neutralizing antibodies to the FVIII and FIX transgene products. Nevertheless, although the preclinical paradigm of hemophilic mouse followed by...
MEDICAL DESCRIPTORS:
disease model; prediction; hemophilia A--drug therapy--dt; **hemophilia B** --drug therapy--dt; somatic cell; phenotype; drug efficacy; drug safety; drug design; virus vector; toxicity; dog; drug screening; gene targeting; gene expression; drug infusion; gene...

10/3,K/16 (Item 2 from file: 73)

12607026 EMBASE No: 2004199157

Nonviral gene therapy approaches to hemophilia

Gomez-Vargas A.; Hortelano G.
Dr. G. Hortelano, Dept. of Pathol. and Molec. Medicine, McMaster University, Hamilton, Ont. L8N 3Z5 Canada
AUTHOR EMAIL: gonhort@mcmaster.ca
Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (197-204)
CODEN: STHMB ISSN: 0094-6176
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 92

The goal of hemophilia gene therapy is to obtain long-term therapeutic levels of **factor VIII** (FVIII) or factor IX (FIX) without stimulating an immune response against the transgene product or the **vector** . The success of gene therapy is largely dependent on the development of appropriate gene delivery vectors. Both viral vectors and nonviral vectors have been considered...
MEDICAL DESCRIPTORS:
...transgene; gene delivery system; virus vector; drug efficacy; disease model; inflammation; gene expression; risk assessment; carcinogenesis; cancer risk; randomization; phenotype; hemophilia A--drug therapy--dt; **hemophilia B** --drug therapy--dt; drug formulation; genome; gene transfer; liver; electroporation; injection; drug targeting; drug delivery system; target cell; ex vivo study; transposon; gene mutation; human...

10/3,K/17 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

12607025 EMBASE No: 2004199156
Onco-retroviral and lentiviral vector-based gene therapy for hemophilia: Preclinical studies
Van Damme A.; Chuah M.K.L.; Collen D.; VandenDriessche T.
Dr. T. VandenDriessche, University of Leuven, Flanders Interuniv. Inst. Biotech., University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven Belgium
AUTHOR EMAIL: thierry.vandendriessche@med.kuleuven.ac.be
Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (185-195)
CODEN: STHMB ISSN: 0094-6176
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 96

Hemophilia A and B gene therapy requires long-term and stable expression of coagulation **factor VIII** (FVIII) or factor IX (FIX), respectively, and would need to compare favorably with protein replacement therapy. Onco-retroviral and lentiviral vectors are attractive vectors for...

...remain a major issue that must be resolved before the full potential of these vectors eventually can be exploited clinically. Nevertheless, the continued progress in **vector** design combined with a better understanding of **vector** biology may ultimately yield more effective gene therapy approaches using these integrating vectors.
MEDICAL DESCRIPTORS:
retrovirus vector; lentivirus vector; hemophilia A--drug therapy--dt; **hemophilia B** --drug therapy--dt; protein expression; target cell; genome; genetic transduction; cell type; cell division; ex vivo study; in vivo study; evaluation; gene delivery system; liver...

10/3,K/18 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

12607023 EMBASE No: 2004199154
Preclinical gene therapy studies for hemophilia using Adeno-Associated Virus (AAV) vectors
Couto L.B.
Dr. L.B. Couto, Couto Consulting, Pleasanton, CA United States
AUTHOR EMAIL: coutoconsulting@yahoo.com
Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (161-171)
CODEN: STHMB ISSN: 0094-6176
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 57

...IX (FIX), although the levels vary. Intrahepatic delivery is more efficacious than intravenous administration, which is superior to intramuscular delivery. The recent development of efficient **factor VIII** (FVIII) expression cassettes has made AAV-based gene therapy for hemophilia A also within reach. Although no acute toxicity has been observed with any route of administration, an increased risk of antibody formation against

FIX has been noted following intramuscular delivery. Biodistribution studies concluded that the **vector** disseminates to most tissues in a dose-dependent and time-dependent manner, but the majority of the **vector** resides in the targeted tissue. In addition, the risk of germline transmission has been shown to be low or absent. The relatively recent isolation of...

...be addressed. Delivery of AAV to large animals has not been reproducible, which could be due to nonoptimized delivery and/or immune responses to the **vector** or transgene product. In addition, a complete understanding of the biology of these vectors is required to assess their long-term safety. Solving these issues...
MEDICAL DESCRIPTORS:
...safety; disease model; drug efficacy; drug administration route; antibody production; risk assessment; dose time effect relation; virus isolation; serotype; immune response; drug delivery system; transgene; **hemophilia B** --drug therapy--dt; dose response; hemostasis; liver; drug potency; gene expression; peripheral vein; hemophilia A--drug therapy--dt; toxicity; drug tolerability; drug bioavailability; mutagenesis; human...

10/3,K/19 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

11292970 EMBASE No: 2001308599
Gene therapy of hemophilia
Schwaab R.; Oldenburg J.
Dr. R. Schwaab, Inst. Exp. Haematol./Transfus. Med., Sigmund-Freud-Str. 25, 53105 Bonn Germany
AUTHOR EMAIL: rainerschwaab@ukb.uni-bonn.de
Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2001, 27/4 (417-424)
CODEN: STHMB ISSN: 0094-6176
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 50

Hemophilia A and B are X-linked bleeding disorders caused by mutations within the **factor VIII** and factor IX genes, respectively. Although both disorders can be easily treated by substitution with concentrates of functional **factor VIII** and factor IX, considerable effort has been undertaken to develop a gene therapy for hemophilia in order to improve patients' life quality and reduce high costs of therapy. The principle of gene therapy is the introduction of an intact copy of the **factor VIII** /factor IX gene in somatic cells, compensating for the defective gene. To do this, retroviral, adenoviral, and adeno-associated virus (AAV) **vector** systems, among others, were used. Encouraged by the results of preliminary experiments using preponderant mouse and canine models, three clinical phase I studies on hemophilia...
MEDICAL DESCRIPTORS:
*hemophilia A--disease management--dm; *hemophilia A--drug therapy--dt; * hemophilia A--etiology--et; * **hemophilia B** --disease management--dm; * **hemophilia B** --drug therapy--dt; * **hemophilia B** --etiology--et; *gene therapy
?

Set	Items	Description
S1	2	(HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)

```
S2          2   RD  (unique items)
S3        457   (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
S4         21   S3  (S) (PULMONARY OR LUNG OR INTRANASAL)
S5          0   S4 AND (HEMOPHILIA (W) B)
S6         11   RD S4  (unique items)
S7         30   S3 AND (HEMOPHILIA (W) B)
S8          0   S7 AND (PULMONARY OR LUNG OR INTRANASAL)
S9         19   RD S7  (unique items)
S10        19   S9 NOT S6
?

COST
       04apr06 15:40:16 User259876 Session D859.2
            $3.04    0.894 DialUnits File155
               $4.18  19 Type(s) in Format  3
            $4.18  19 Types
     $7.22  Estimated cost File155
            $5.57    0.945 DialUnits File5
               $1.12  7 Type(s) in Format 95 (KWIC)
            $1.12  7 Types
      $6.69  Estimated cost File5
            $8.97    0.801 DialUnits File73
              $18.60  6 Type(s) in Format  3
           $18.60  6 Types
     $27.57  Estimated cost File73
            OneSearch, 3 files,  2.640 DialUnits FileOS
      $3.46  INTERNET
     $44.94  Estimated cost this search
     $45.81  Estimated total session cost   2.873 DialUnits
?
```

Return to logon page!